VA | U.S. Department of Veterans Affairs
Veterans Health Administration
Corporal Michael J. Crescenz VA Medical Center

Penn Medicine

Neurological Manifestations Following Exposure to Directional Phenomena: *Preliminary Findings*

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Disclosure

- Support was provided by the US government in the form of background information and referral of patients
- The findings and conclusions are those of Dr. Swanson and the authors of the JAMA publication, and should not be construed as officially reflecting the views of the Unites States Government, including the Department of State or the Department of Veterans Affairs.
- Dr. Swanson will only be discussing information that was made public in the Senate Subcommittee Hearing dated January 9th 2018, and the recent JAMA publication released February 15th 2018.
- Any other inquiries should be directed to the Department of State, Bureau of Public Affairs at (202) 647-6575

Disclosure

Large Multidisciplinary Team Effort

Clinical Specialties

- ***Physical Medicine & Rehabilitation***
- ***Occupational Medicine***
- ***Neurology***
- ***Neurosurgery***
- ***Neuroradiology / Radiology***
- Neuropsychology
- Neuro-Optometry
- Neuro-Ophthalmology
- Audiology / Otorhinolaryngology
- Sleep Medicine
- Epidemiology / Biostatistics

Rehabilitation Specialists

- Vestibular Therapy
- Occupational Therapy
- Speech Language Pathology
- Neuro-optometric Rehabilitation

Over 25 Specialists involved in the evaluation and treatment of this patient cohort

Outline

- Introduction / Background / Timeline
- Exposure reports
- Neurological Manifestations
- Neurological Rehabilitation: approach and preliminary response
- Future Directions

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UNITED STATES SENATE COMMITTEE ON FOREIGN RELATIONS

Subcommittee Hearing Attacks on U.S. Diplomats in Cuba: Response and Oversight

January 9, 2018; 10:00 AM; SD-419; **Presiding:** Senator Rubio

WITNESSES

1. **Mr. Francisco Palmieri**

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United States Department of State

Washington , D.C.

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2. **Mr. Todd Brown**

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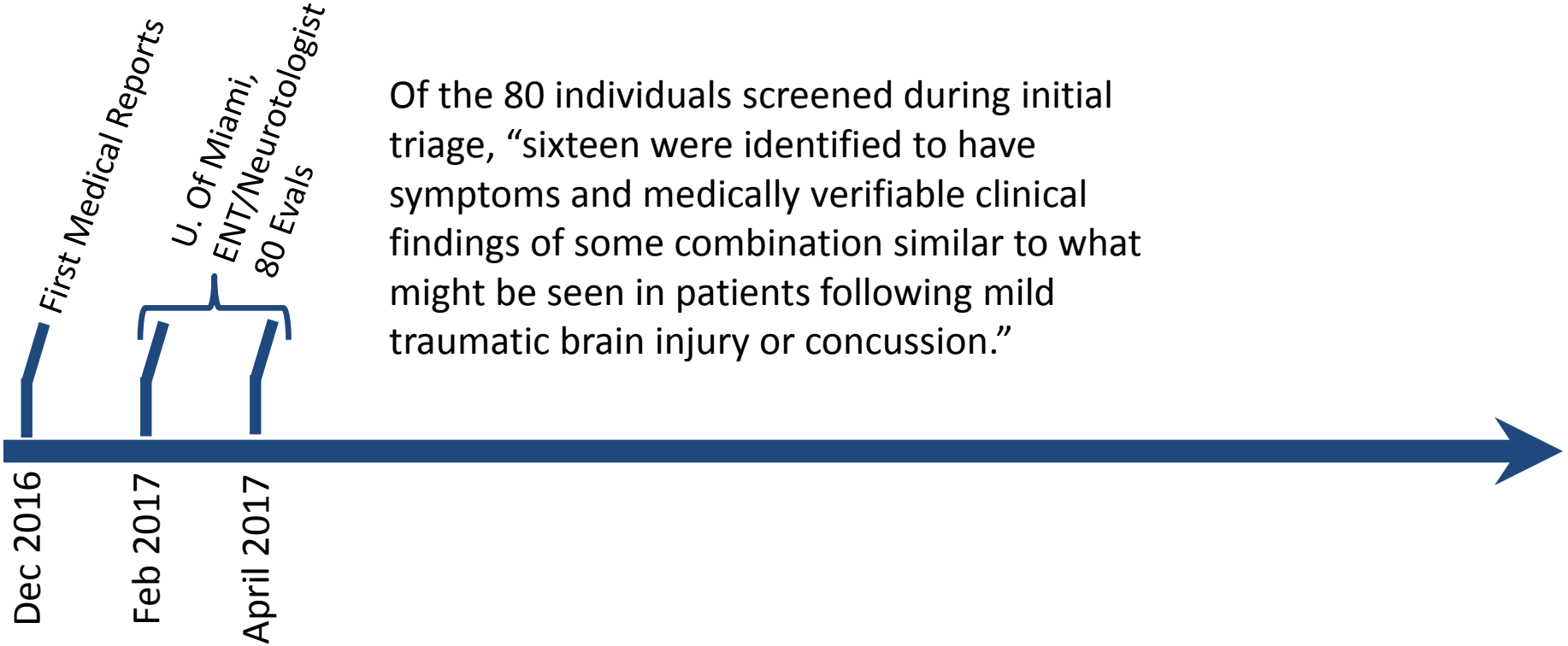

Of the 80 individuals screened during initial triage, “sixteen were identified to have symptoms and medically verifiable clinical findings of some combination similar to what might be seen in patients following mild traumatic brain injury or concussion.”

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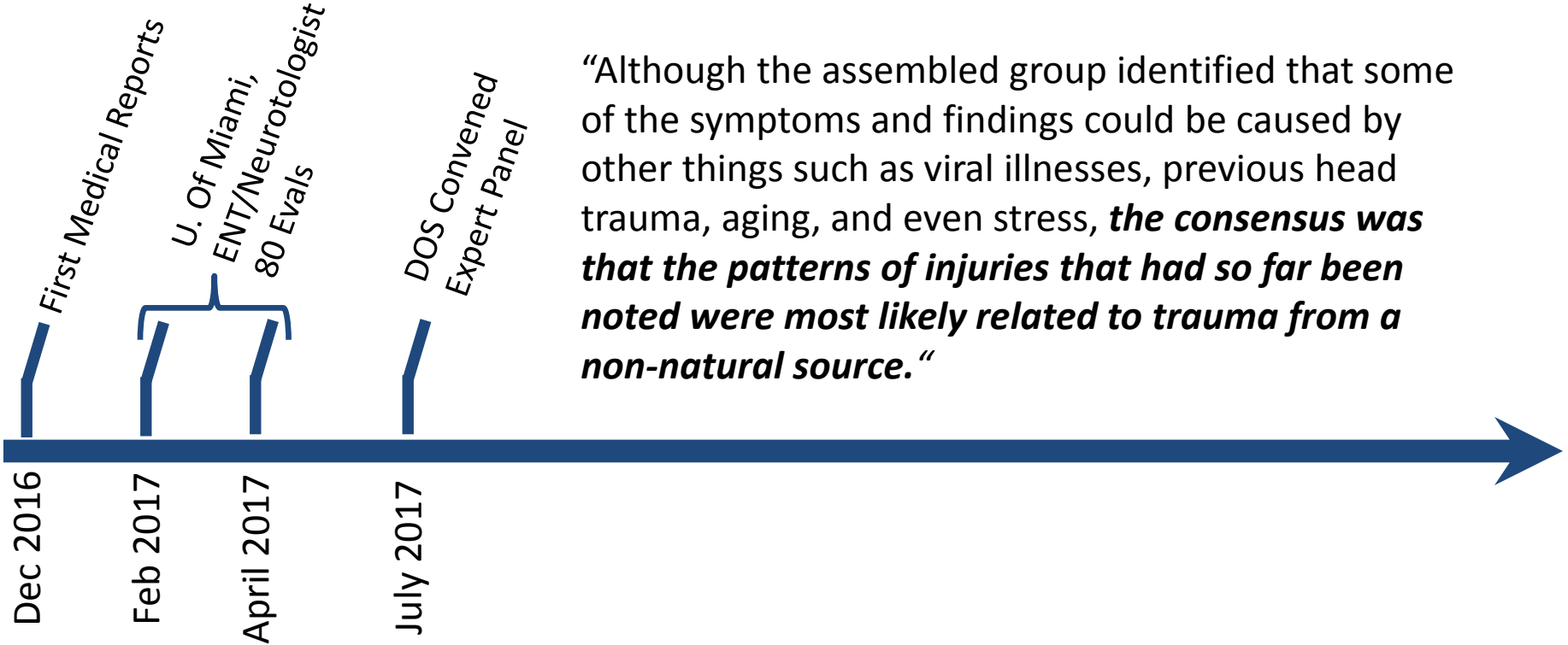

"Although the assembled group identified that some of the symptoms and findings could be caused by other things such as viral illnesses, previous head trauma, aging, and even stress, ***the consensus was that the patterns of injuries that had so far been noted were most likely related to trauma from a non-natural source.***"

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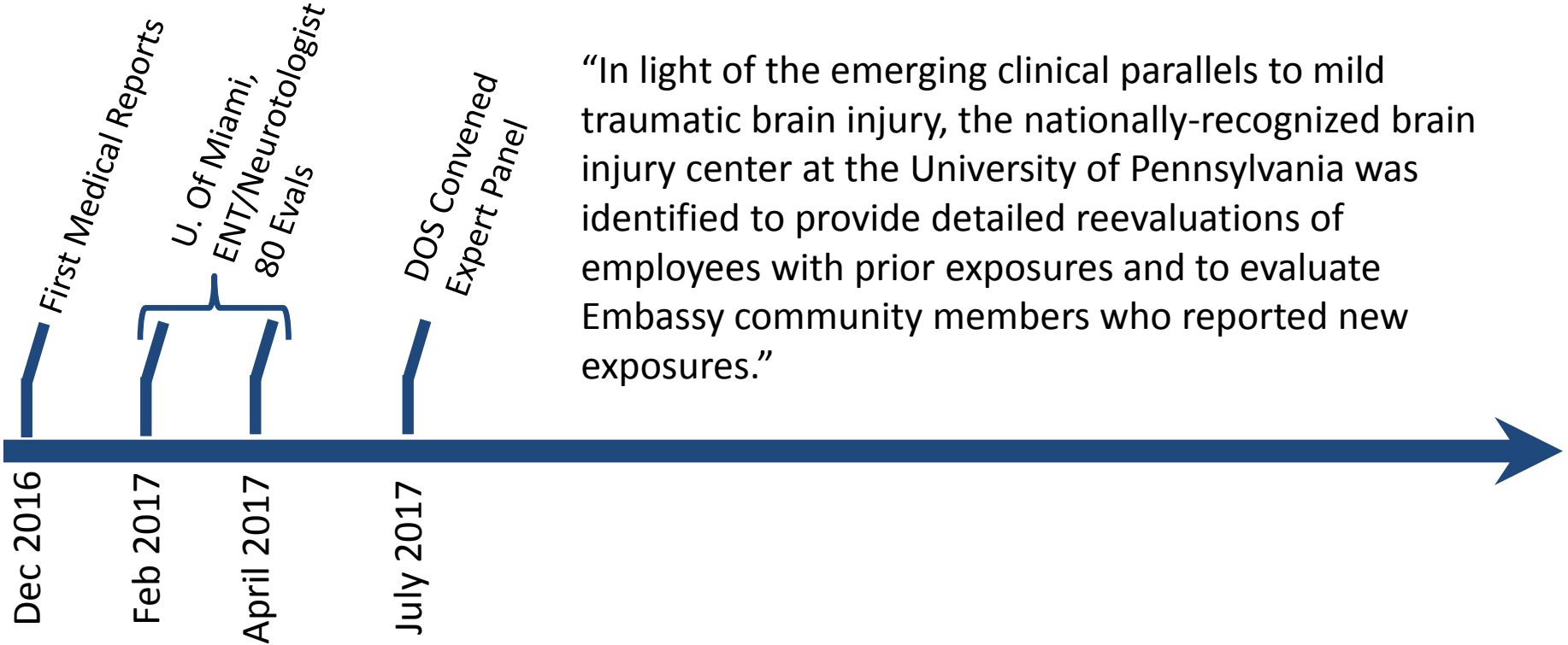

"In light of the emerging clinical parallels to mild traumatic brain injury, the nationally-recognized brain injury center at the University of Pennsylvania was identified to provide detailed reevaluations of employees with prior exposures and to evaluate Embassy community members who reported new exposures."

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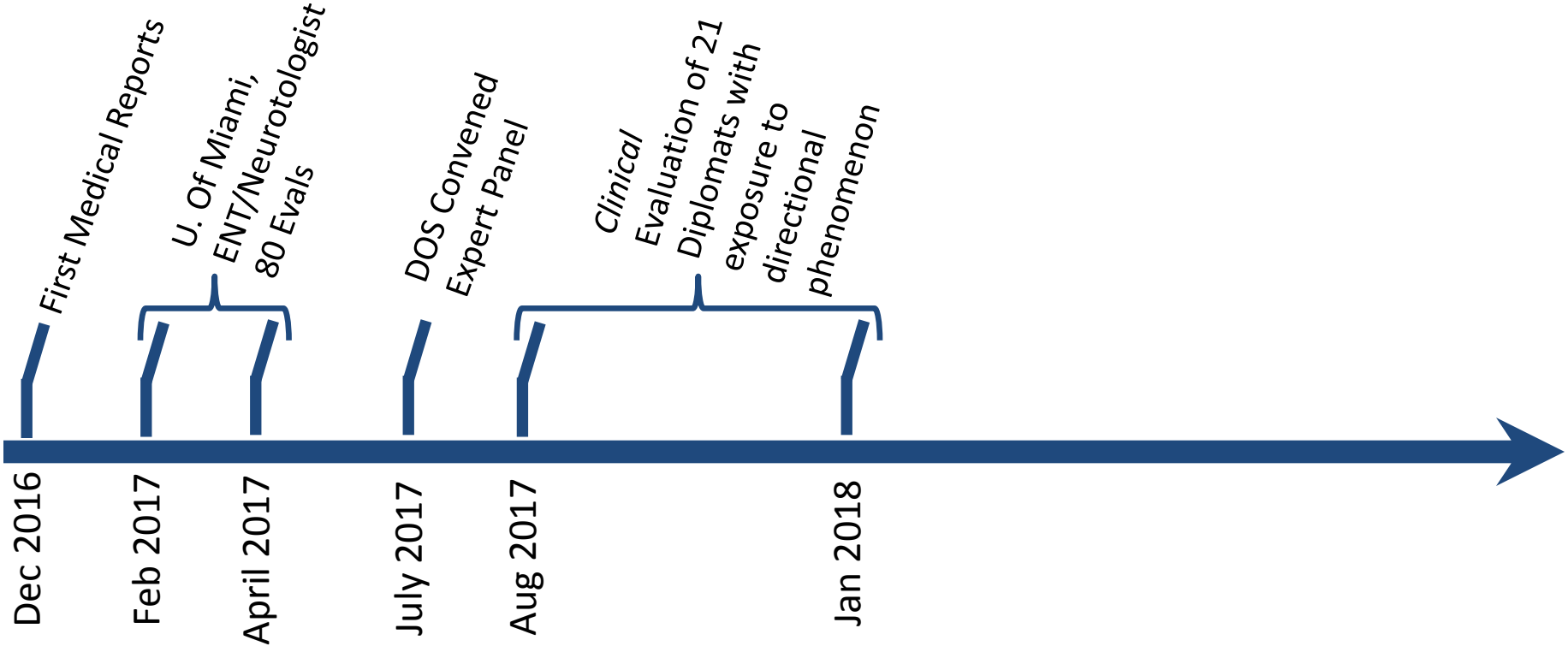

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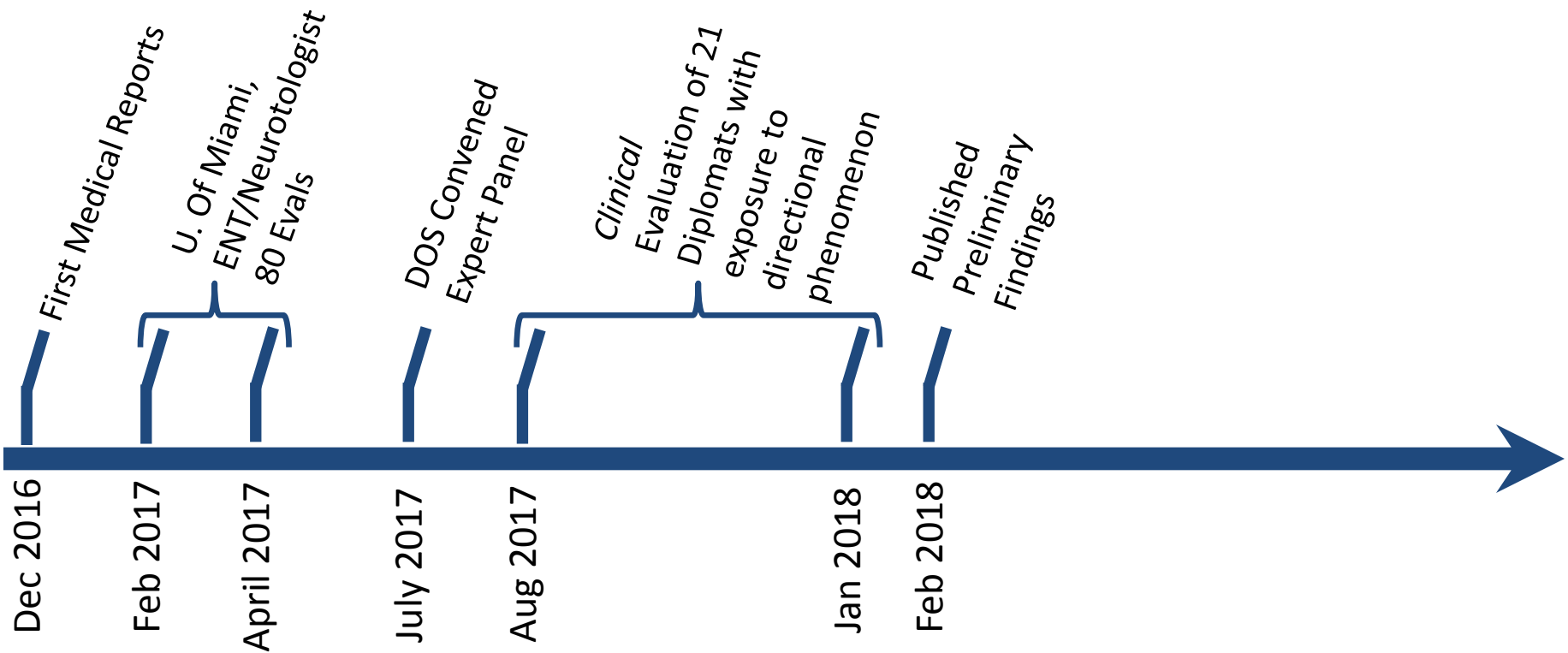

JAMA | Preliminary Communication

Neurological Manifestations Among US Government Personnel Reporting Directional Audible and Sensory Phenomena in Havana, Cuba

Randel L. Swanson II, DO, PhD; Stephen Hampton, MD; Judith Green-McKenzie, MD, MPH; Ramon Diaz-Arrastia, MD, PhD; M. Sean Grady, MD; Ragini Verma, PhD; Rosette Biester, PhD; Diana Duda, PT, DPT; Ronald L. Wolf, MD, PhD; Douglas H. Smith, MD

IMPORTANCE From late 2016 through August 2017, US government personnel serving on diplomatic assignment in Havana, Cuba, reported neurological symptoms associated with exposure to auditory and sensory phenomena.

OBJECTIVE To describe the neurological manifestations that followed exposure to an unknown energy source associated with auditory and sensory phenomena.

DESIGN, SETTING, AND PARTICIPANTS Preliminary results from a retrospective case series of US government personnel in Havana, Cuba. Following reported exposure to auditory and

Editorial
Author Audio Interview
Related article
Supplemental content

JAMA. doi:10.1001/jama.2018.1742
Published online February 15, 2018.

Demographics

Table 1. Demographics of Patients Evaluated at the University of Pennsylvania[a]

	Men (n = 10)	Women (n = 11)	Total (N = 21)
Age, mean (SD), y	39 (7)	47 (8)	43 (8)
Time from exposure to evaluation, mean (SD), d	229 (98)	180 (85)	203 (93)

Range: 3-331 days
Median: 189 days
interquartile range: 125 days

[a] Potentially identifying information intentionally omitted for security and privacy concerns.

Outline

- Introduction / Background / Timeline
- **Exposure reports**
- Neurological Manifestations
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Exposure Reports

Table 2. Exposure Descriptions of the Directional Phenomena

Patient No.	Associated Sound			Associated Sensory Stimuli				Duration >3 mo		
	Reported	High Pitch	Low Pitch	Reported	Pressure	Vibration	Movement Attenuation[a]	Persistent Symptoms	Objective Findings	Required Treatment
1	X	X					X	X	X	X
2	X	X					X	X	X	X
3	X	X					X			
4	X		X	X		X		X	X	X
5	X	X		X	X			X	X	X
6	X		X	X	X		X	X	X	X
7				X	X		X	X		
8	X	X					X	X	X	X
9	X	X		X		X		X	X	X
10	X	X		X		X		X	X	X
11	X	X		X	X			X	X	X
12	X	X		X	X			X	X	X
13	X	X					X	X	X	X
14	X	X					X	X	X	X
15	X	X		X	X		X	X	X	X
16	X	X					X	X	X	X
17	X	X		X	X		X	X	X	X
18								X	X	X
19	X	X		X	X			X		
20				X	X		X	X	X	X
21	X	X						X	X	X
No. (%)	18 (86)	16 (76)	2 (10)	12 (57)	9 (43)	3 (14)	12 (57)	20 (95)	18 (86)	18 (86)

[a] Patients reported attenuation of sound, pressure, or vibration when moving to a different location.

Exposure Reports

Domain	Acute	n	(%)	Subacute	n	(%)
Cognitive / Behavioral	**Combined**	**16**	**(76)**	**Combined**	**19**	**(90)**
	Desire to change location	10	(48)	Cognitive change	13	(62)
	Confusion/Disorientation	8	(38)	Memory trouble	11	(52)
	Agitation/Irritability	6	(29)	Difficulty concentrating	11	(52)
	Desire to cover head/ears	5	(24)	Word finding difficulty	11	(52)
	Fatigue	3	(14)	Fatigue	10	(48)
	Feeling of paralysis	3	(14)	Agitation/Irritability	8	(38)
				Increased time for cognitive tasks	7	(33)
				Errors at work	6	(29)
Balance / Vestibular	**Combined**	**10**	**(48)**	**Combined**	**14**	**(67)**
	Nausea	**7**	(33)	Dizziness	13	(62)
	Dizziness	**5**	(24)	Falls	4	(19)
				Nausea	3	(14)
Visual	**Combined**	**2**	**(10)**	**Combined**	**14**	**(67)**
	Visual changes	**1**	(5)	Visual changes	10	(48)
	Eye pain	**1**	(5)	Light sensitivity	**9**	**(43)**
				Eye strain	7	(33)
				Difficulty focusing vision	**6**	**(29)**
Auditory	**Combined**	**10**	**(48)**	**Combined**	**15**	**(71)**
	Ear pain	7	(33)	Tinnitus	12	(57)
	Tinnitus	6	(29)	Hearing change	7	(33)
	Hearing change	1	(5)	Noise sensitivity	5	(24)
				Ear pain	5	(24)
Sleep	**Sleep problem**	**4**	**(19)**	**Sleep problem**	**16**	**(76)**
Headache	**Combined**	**11**	**(50)**	**Combined**	**17**	**(81)**
	Headache	8	(38)	Headache	17	(81)
	Head Pressure	5	(24)	Unilateral jaw pain	2	(10)
	Unilateral jaw pain	1	(5)			
Overall	**Combined acute**	**21**	**(100)**	**Combined subacute**	**21**	**(100)**

Acute – during or hours following exposure, Subacute – days to weeks following exposure
Developed from patient descriptions of symptoms in acute and subacute period following exposure during evaluations at the University of Pennsylvania. Clinical interviews were open-ended, therefore lack of a particular symptom was not systematically verified

Audience Response Question #1:

Question

- Over half of the patients reported attenuation of acute symptoms when they moved away from the perceived directional phenomena.
  A. True
  B. False

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Neurological Manifestations

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Neurological Manifestations

PM&R Brain injury H&P

- Detailed HPI, including symptom scales, h/o past neurological insults
- Comprehensive physical examination
    - with focus on cognitive, oculomotor and vestibular examination

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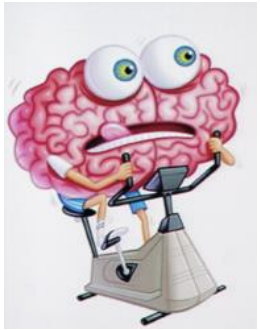
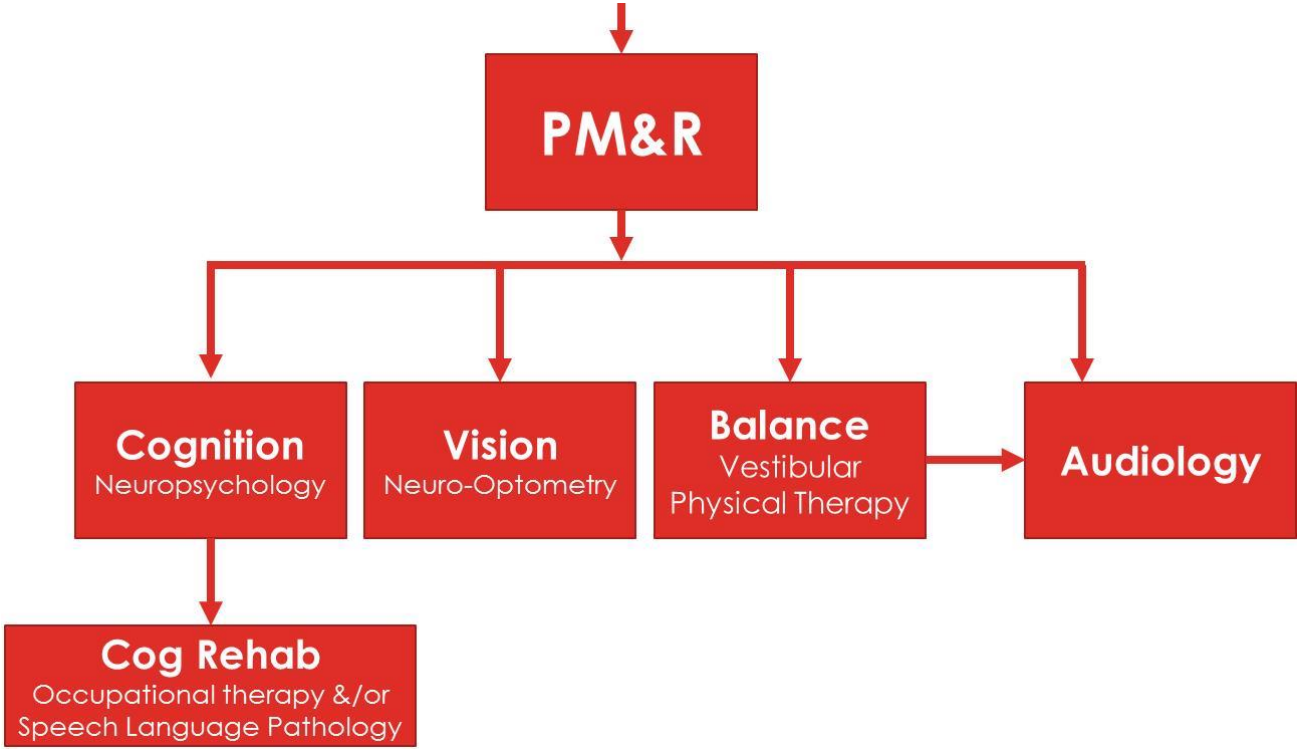


mTBI sTBI

Neurological Manifestations



Neurological Manifestations

Table 3. Prevalence of Persistent Symptoms and Objective Findings[a]

	Subjective		Objective	
Domain	Symptom	No. (%)	Finding	No. (%)
Cognitive and behavioral	Combined	17 (81)	Neuropsychological testing indicated	16 (76)[b]
	Difficulty remembering	16 (76)	Neuropsychological testing performed at Penn	10 (48)
	Mental fog	16 (76)	Neuropsychological testing outside Penn	4 (19)
	Difficulty concentrating	15 (71)	Neuropsychological testing not yet performed	2 (10)
	Feeling slowed	14 (67)	Cognitive rehabilitation	13 (62)[b]
	Irritability	14 (67)		
	Feeling more emotional	11 (52)		
Balance and vestibular	Combined	15 (71)	Vestibular physical therapy referral	17 (81)
	Balance problems	14 (67)	Static postural stability	16 (76)
	Dizziness	13 (62)	Dynamic balance	16 (76)
	Nausea	7 (33)	VOR dysfunction	15 (71)
			Unilateral caloric impairment	4 (31)[c]
			Vestibular rehabilitation	17 (81)
Vision and oculomotor	Combined	18 (86)	Neuro-optometry referral	15 (71)
	Visual problems	16 (76)	Convergence insufficiency	11 (52)
	Light sensitivity	13 (62)	Smooth pursuit dysfunction	11 (52)
	Difficulty reading	12 (57)	Saccadic dysfunction	10 (47)
	Eye strain	11 (52)	Neuro-optometric rehabilitation	14 (67)

Neurological Manifestations

Table 3. Prevalence of Persistent Symptoms and Objective Findings[a]

Auditory	Combined	15 (68)	Audiology referral	13 (62)
	Sound sensitivity	14 (67)	Moderate to severe SNHL	3 (23)[c]
	Tinnitus	12 (57)	Hearing aid provided	3 (14)
	Hearing reduction	9 (43)		
	Ear pressure	8 (38)		
Sleep	Combined	18 (86)	Pharmacological intervention	15 (71)
	Drowsiness or fatigue	16 (76)		
	Decreased sleep duration	15 (71)		
	Trouble falling asleep	14 (67)		
Headache	Combined	16 (76)	Pharmacological intervention	12 (57)
	With cognitive tasks	13 (62)		
	With therapy	11 (52)		
	Due to photophobia	9 (43)		
	Due to phonophobia	6 (29)		
Overall	Combined subjective	20 (95)	Combined objective	18 (86)

Neurological Manifestations

Table 3. Neuropsychological Test Results: Effort Testing (n=6)

	Case					
	4	**9**	**11**	**13**	**15**	**20**
Effort						
Test of Memory Malingering						
Trial 1	50	50	50	50	42	41
Trial 2	50	50	50	50	50	50
Rey 15-Item Visual Memory Test	15	15	15	15	12	15

Values listed are all raw values, not percentiles

- *For the Test of Memory Malingering,[4-6] normal is >26 on trial 1 and >45 on Trial 2*
- *For Rey 15-Item Visual Memory Test,[7-11] a score of <9 is interpreted as a lack of effort*

eTable 2. Neuropsychological Test Results: Cognitive Domains (n=6)

	Case					
	4	**9**	**11**	**13**	**15**	**20**
Auditory Attention and Working Memory						
Digit Span Forward	50	84	**9**	91	50	98
Digit Span Backward	63	63	50	95	**16**	95
Digit Span Sequencing	37	**37**	50	95	**37**	75
Arithmetic	91	50	**37**	98	**25**	75
Letter-Number Sequencing	63	50	63	99	**37**	50
Visual Working Memory						
Symbol Span	63	50	84	75	63	95
Auditory and Visual Memory						
Logical Memory I	84	**9**	75	91	50	50
Logical Memory II	63	**16**	**37**	95	50	50
Verbal Paired Associates I	95	**37**	91	98	63	63
Verbal Paired Associates II	91	**37**	91	95	50	50
Designs I	91	**9**	50	84	91	84
Designs II	91	**25**	63	91	75	75
Visual Reproduction I	75	50	**25**	98	**16**	63
Visual Reproduction II	91	36	75	95	**25**	50
Rey-Osterrieth Complex Figure: 3-minute delay	95	**15**	**<10**	65	40	**<10**
California Verbal Learning Test – II: Trials 1 – 5	84	88	84	97	95	95
California Verbal Learning Test – II: Long Delay	63	84	50	94	**25**	**<1**
Visual-Spatial Perception and Visual-Motor Construction						
Judgment of Line Orientation	>86	72	56	>86	40	**2**
Rey-Osterrieth Complex Figure - copy	100	**<10**	**<10**	**20**	90	60
Block Design	91	63	**16**	91	75	75
Motor Functions						
Grooved Pegboard: Dominant	44	**16**	**<1**	88	**19**	**<1**
Grooved Pegboard: Non-Dominant	**30**	**16**	**2**	88	**9**	50
Language Functioning						
Boston Diagnostic Aphasia Examination: Boston Naming Test	88	50	**19**	**7**	**25**	65
Boston Diagnostic Aphasia Examination: Complex Ideational Material	58	50	**19**	50	50	50
Vocabulary	63	63	75	84	63	75
Executive Functions						
Controlled Oral Word Association: FAS	96	**39**	88	**9**	58	96
Animal Naming	58	55	**19**	**4**	60	60
Trail Making Test: Part A	**21**	65	88	82	97	**<1**
Trail Making Test: Part B	**25**	**34**	**19**	**30**	65	**<1**
Ruff Figural Fluency Test: Total Designs	61	**32**	**29**	81	**21**	59
Ruff Figural Fluency Test: Perseverative Errors	63	64	**19**	52	63	63
Processing Speed						
Coding	63	**37**	**37**	91	84	**16**
Symbol Search	63	**25**	63	**37**	84	**2**
Academic Achievement						
Wide Range Achievement Test-4, Word Reading	47	50	61	68	63	61
Reasoning						
Similarities	63	63	**37**	95	50	84
Matrix Reasoning	84	75	50	75	75	63
Visual Puzzles	95	84	**5**	98	63	75

Percentile scores shown. Bold highlighting denotes abnormality or <40th percentile[1-3]

Neurological Manifestations

Table 4. Neuropsychological Test Results: Mood Functioning (n=6)

	Case					
	4	**9**	**11**	**13**	**15**	**20**
Mood Functioning[12-17]						
Beck Depression Inventory-II	3 (Min)	17 (Mild)	**24 (Mod)**	12 (Min)	11 (Min)	16 (Mild)
Beck Anxiety Inventory-Revised	2 (Min)	2 (Min)	14 (Mild)	10 (Mild)	5 (Min)	10 (Mild)
Brief Mood Survey						
Depression	0	2 (Bord)	**7 (Mod)**	3 (Mild)	3 (Mild)	3 (Mild)
Suicidal Urges	0	0	0	0	0	0
Anxiety	1 (Bord)	3 (Mild)	**11 (Severe)**	3 (Mild)	4 (Mild)	5 (Mild)
Panic	ND	0	2 (Bord)	1 (Bord)	ND	0
Anger	1 (Bord)	**11 (Severe)**	**13 (Severe)**	4 (Mild)	4 (Mild)	4 (Mild)
Post-Traumatic Stress Disorder Checklist - 5 *(Cutoff score 33)*	1	**36**	**49**	23	16	23
Frontal Systems Behavior Scale *(Before/After Injury)*						
Apathy	41/46	**43/77**	**53/92**	**47/69**	**42/68**	**48/66**
Disinhibition	36/44	**57/67**	49/55	**50/66**	39/43	37/45
Executive Dysfunction	41/45	**39/67**	**41/76**	44/56	**46/68**	**47/75**
Total	37/44	**44/74**	**47/74**	46/64	41/62	43/65

Values listed are all raw values, not percentiles
Bold highlighting denotes abnormality
Abbreviations: Minimal (Min), Borderline (Bord), Not done (ND)

Neurological Manifestations

eTable 5. Standardized Measures Obtained During Initial Vestibular Physical Therapy Evaluation

	Self-Reported Measures		Objective Measures		
Case	DHI	ABC	FGA	BESS	SOT
1	**38**	---	**29**	**39**	**41**
2	18	90	**29**	7	78
4	**38**	84	**28**	**24**	71
5	**38**	84	**23**	**30**	**59**
6	**50**	**64**	**20**	**42**	78
8	10	88	**29**	**30**	**45**
9	24	76	**27**	**41**	**43**
10	**56**	76	**24**	**34**	73
11	**60**	76	**28**	**23**	**52**
12	---	---	30	**16**	**68**
13	26	86	**21**	**30**	**48**
15	20	---	**29**	**16**	**61**
16	24	93	**25**	**50**	**UTC**
17	**58**	**61**	**18**	**UTC**	**UTC**
18	**30**	88	30	14	**45**
20	**60**	79	**29**	**41**	**20**
21	18	86	**26**	**29**	**56**

Normative values
- DHI[18]: Mild (0-30), Moderate (31-60), Severe (61-100) vestibular dysfunction
-ABC[19]: Score < 67% indicates a risk of falling
- FGA[20]: Normal is 30/30
- BESS[21]: Normative values used based on Iverson et al 2013[22], yielding a categories (superior, above average, broadly normal, below average, poor, and very poor) based on age and sex. Scored 0-60, with higher scores indicating increased static balance impairment.
-SOT[23]: Cut off was 70 for equilibrium score for all patients in the age group tested
- Bold highlighting denotes abnormality
-Abbreviations: Dizziness Handicap Index (DHI); Activities Balance Confidence Scale (ABC); Functional Gait Assessment (FGA); Balance Error Scoring System (BESS); Neurocom Balance Manager Sensory Organization test (SOT), Unable to complete (UTC)

eTable 6. Caloric Testing Results

	Cool		Warm		RVR*	
Case	Right	Left	Right	Left	%	R/L
1	35	33				
5	23	20				
8	34	22	27	24	7	L
9	20	20				
10	9	3	12	4	**50**	**L**
11	24	13	19	7	**37**	**L**
13	12	22	22	28		
15	28	17	38	20	**28**	**L**
16	39	48	51	62	10	R
17	18	22				
18	19	20				
20	37	8	63	12	**67**	**L**
21	42	35				

Normal Values: RVR threshold is <25% asymmetry. Above 25% asymmetry is diagnostic for a unilateral peripheral vestibular lesion.[24-26]
– *Bold highlighting denotes abnormality*
- Abbreviation: Relative Vestibular Reduction (RVR)
- Evaluation of warm caloric and RVR only indicated when asymmetry observed with cool caloric per standard audiology practice.

Neurological Manifestations

eTable 7. Vestibular Impairments Identified Requiring Rehabilitation Interventions

Case	Static Balance	Dynamic Balance	VOR+ Impairment	Unilateral Peripheral Vestibular Impairment
1	X	X	X	
2		X	X	NT
4	X	X		NT
5	X	X	X	
6	X	X	X	NT
8	X	X	X	
9	X	X	X	
10	X	X	X	X
11	X	X	X	X
12	X			NT
13	X	X	X	
15	X	X	X	X
16	X	X	X	
17	X	X	X	
18	X	X	X	
20	X	X	X	X
21	X	X	X	
n	16	16	15	4
(%)	(76)	(76)	(71)	(31)*

+ Vestibulo-ocular reflex (VOR)
*Percentage is based on 13 individuals who underwent caloric evaluation
Abbreviations: Not tested (NT)

Neurological Manifestations

eTable 8. Standardized Measures Obtained During Initial Neuro-Optometry Evaluation

	Self-Reported Measure	Objective Measures			
		NPC (cm)			
Case	CISS*	Break	Recovery	PFV (PD)	DEM (sec)
1	**40**	**7.5**	**13**	35	29
2	---	2.5	5	25	25
4	---	2.5	5	25	**32**
5	**76**	**13**	**20**	**12**	**40**
6	---	**10**	**15**	30	27
9	**40**	**12**	**23**	**20**	**53**
10	---	4	7.5	40	27
11	**74**	**7.5**	**13**	**16**	**58**
13	**51**	**10**	**15**	**18**	**40**
14	---	5	7.5	30	**50**
15	**46**	**13**	**25**	**6**	**40**
16	**77**	**7.5**	**15**	30	**74**
17	**67**	**25**	**40**	**18**	**67**
18	---	5	8	**18**	**38**
20	**57**	**7.5**	**30**	**6**	**90**

Normative values

- Abnormal CISS[27] is >= 16
- Abnormal NPC[28,29] is >= 6cm break and >=8cm for Recovery
- Abnormal PFV[28,29] <=20 prism diapters (PD) base out.
- Abnormal DEM[28,30] is >= 30 seconds

- Bold highlighting denotes abnormality

-Abbreviations: Convergence Insufficiency Symptom Survey (CISS); Near Point of Convergence (NPC); Positive Fusional Vergence (PFV); Prism Diopters (PD); Developmental Eye Movement Test (DEM)

* CISS obtained at initiation of neuro-optometric rehabilitation when indicated per standard neuro-optometry practice.

Neurological Manifestations

eTable 9. Clinically Significant Oculomotor Impairments Identified Requiring Dedicated Neuro-optometric Rehabilitation (n=11)

Case	Convergence Insufficiency	Accommodative Insufficiency	Saccadic Dysfunction	Pursuit Dysfunction	Photophobia
1	X	*		X	X
5	X	*	X	X	X
6	X			X	X
9	X	*	X		
11	X	X	X	X	X
13	X	*	X	X	X
15	X	*	X	X	X
16	X	X	X	X	X
17	X	*	X	X	X
18	X		X	X	
20	X	*	X	X	X
n	11	2	9	10	9
(%)	(100)	(18)	(82)	(91)	(82)

*Measurements consistent with accommodative insufficiency and historical description of visual change after exposure, however formal diagnosis limited over the age of 40 due to age-appropriate presbyopia.
-clinical diagnosis of convergence insufficiency, accommodative insufficiency, saccadic and pursuit dysfunction, and photophobia was performed according to the standards detailed in the methods section, and included integration of standardized measures along with expert clinical evaluation.
-of the 4 individuals listed in Table 1 above that did not require formal Neuro-optometric rehabilitation at Penn, one received neuro-optometric rehabilitation after exposure but prior to Penn evaluation, two had oculomotor exercises integrated into vestibular and/or occupational therapy, and was provided a home exercise program.

Neurological Manifestations – Clinical Correlation

VOMS (Vestibular Ocular Motor Screening)

- Pursuits
- Saccades
- Near Point of Convergence (NPC) – 3 reps
- Vestibular Ocular Reflex (VOR)
- Motion sensitivity/VOR cancellation

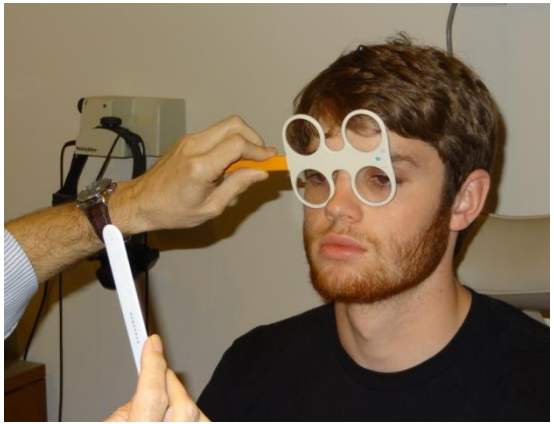
Sx: 1 to 10, dizziness, fogginess, headache, nausea

Mucha, Collins et al. A Brief Vestibular/Ocular Motor Screening (VOMS) assessment to evaluate concussions: preliminary findings. Am J Sports Med. 2014 Oct;42(10):2479-86.

Neurological Manifestations – Clinical Correlation

Neuro-Optometry Evaluation

- Symptoms (Convergence Insufficiency Symptom Survey (CISS)
- Distance VA
- Binocular Vision Testing
  - Maddox Wing
  - Near Point of Convergence
  - (NPC)
  - Step Vergence
  - Vergence facility
- Accommodative testing
  - Accommodative amplitude
  - Accommodative facility
- Eye Movement Testing
  - Developmental Eye Movement
  - Test (DEM)



Neurological Manifestations – Clinical Correlation

Prevalence Studies - Summary

	Soldiers			Adult, Civilians		Children
Problem	Goodrich N=46 Mean age=28	Brahm N=124 Mean age=30.5	Stelmack N=192 Mean age=31	Cuiffreda N=160 Mean age=42	Suchoff N= 62 Mean age=49	Master/Scheiman/ Gallaway N= 100 Mean age=14
Convergence Insufficiency (5%)	30%	48%	28%	36%	42%	49%
Accommodative Dysfunction (6%)	22%	48%	47%	41%	10%	50%
Saccadic Dysfunction (?)	20%	23%	9%	57%	40%	29%

Neurological Manifestations – Clinical Correlation

DOS Cohort Oculomotor findings

Combined	18 (86)	Neuro-optometry referral	15 (71)
Visual problems	16 (76)	Convergence insufficiency	11 (52)
Light sensitivity	13 (62)	Smooth pursuit dysfunction	11 (52)
Difficulty reading	12 (57)	Saccadic dysfunction	10 (47)
Eye strain	11 (52)	Neuro-optometric rehabilitation	14 (67)

Neurological Manifestations – Clinical Correlation

Why is the Prevalence of Oculomotor Dysfunction Higher following brain injury than in the general population?

Neurological Manifestations – Clinical Correlation

The neuro-ophthalmology of head trauma

Rachel E Ventura, Laura J Balcer, Steven L Galetta

Lancet Neurol 2014; 13: 1006–16

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Traumatic brain injury (TBI) is a major cause of morbidity and mortality. Concussion, a form of mild TBI, might be associated with long-term neurological symptoms. The effects of TBI and concussion are not restricted to cognition and balance. TBI can also affect multiple aspects of vision; mild TBI frequently leads to disruptions in visual functioning, while moderate or severe TBI often causes structural lesions. In patients with mild TBI, there might be abnormalities in saccades, pursuit, convergence, accommodation, and vestibulo-ocular reflex. Moderate and severe TBI might additionally lead to ocular motor palsies, optic neuropathies, and orbital pathologies. Vision-based testing

100000 people per year.[1,2] Because around half of the circuits in the brain are involved in vision, many aspects of the visual system are vulnerable to moderate, severe, or mild TBI.[3] Not surprisingly, a wide range of visual

the visual system are vulnerable to moderate, severe, or mild TBI.[3] Not surprisingly, a wide range of visual complaints might follow head trauma, including photophobia, double vision, blurred vision, loss of vision,

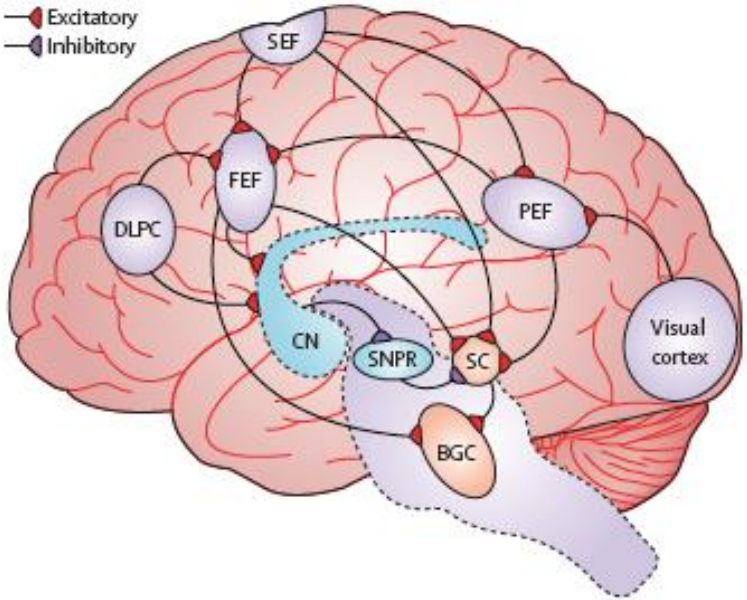
Deficits in visual function in mild TBI

Saccades, antisaccades, and cognitive function

Saccadic eye movements involve a wide variety of cognitive processes and findings from several studies have shown abnormalities in saccade generation after all

Neurological Manifestations – Clinical Correlation

Dysfunction of Neural Networks



Neurological Manifestations – Clinical Correlation

Symptoms of Oculomotor Dysfunction

- Headaches
- Fatigue
- Visual Problems (Blur / Diplopia)
- Dizziness
- Difficulty Reading
- Eye strain

Neurological Manifestations – Clinical Correlation

Symptoms of Oculomotor Dysfunction

	DOS Cohort
• Headaches	• 16/21 (76%)
• Fatigue	• 16/21 (76%)
• Visual Problems (Blur / Diplopia)	• 16/21 (76%)
• Dizziness	• 13/21 (62%)
• Difficulty Reading	• 12/21 (57%)
• Eye strain	• 11/21 (52%)

Neurological Manifestations

eTable 10. Pure Tone Audiometry Results

Case		Frequency (Hz) 250	500	1000	1500	2000	3000	4000	6000	8000
1	R	10	15	10		15	10	10	15	15
	L	10	10	10		5	10	10	15	15
5*	R	15	15	20		20	25	15	5	10
	L	15	15	20		20	20	15	5	5
8	R	10	5	5		10	10	5	10	10
	L	15	10	5		10	15	15	10	5
9†	R	10	5	5		10	**40**	**45**	**30**	20
	L	15	5	10		10	**55**	**35**	20	10
10‡	R	5	10	5		15	**30**	15	5	20
	L	**30**	**35**	**40**	**50**	**55**	**55**	**60**	**75**	**95**
11‡	R	15	15	15		10	15	10	15	5
	L	**50**	**40**	**35**		**30**	**30**	**25**	**25**	10
13§	R	15	15	10		10	15	10	**25**	20
	L	20	20	15		15	20	**25**	**35**	**30**
15	R	5	5	15		10	15	20	20	15
	L	5	15	10		20	15	20	20	20
16	R	20	20	15		20	15	15	15	20
	L	10	15	15		15	15	15	15	15
17§	R	15	20	15		20	**25**	**25**	20	15
	L	20	20	20		10	15	**25**	20	15
18	R	5	10	10		5	10	5	10	10
	L	10	10	5		10	15	10	15	15
20‡	R	**50**	**45**	**45**	**40**	**25**	**25**	**25**	**25**	20
	L	**45**	**45**	**40**	**35**	**25**	**25**	20	**25**	20
21	R	10	15	5		10	5	5	10	10
	L	15	15	15		10	10	5	10	10

Hearing Level in dB

-Results from Pure Tone Audiometry performed as part of a comprehensive audiological assessment which included Speech Audiometry

- NOTE: of the 4 cases with sensorineural hearing loss (SNHL) above (9,10, 11, 20), none of the individuals report noticing or being diagnosed with hearing loss prior to exposure. One individual did report frequent ear infections as a child, though reported normal functional hearing until exposure.

- normal is <=20 dB at each frequency.

- ***Bold highlighting denotes abnormality***

* Case 5: isolated impairment with unclear clinical relevance.

† Case 9: mild to moderate SNHL, no hearing aid indicated.

‡ Cases 10, 11, and 20: moderate to sever SNHL, received hearing aid.

§ Cases 13 and 17: borderline to mild SNHL, no hearing aid indicated.

Neurological Manifestations

eTable 11. Sleep and Headache Medication Requirements

Case	Impaired Sleep		Headache	
	Subjective Complaint	Medication Required	Subjective Complaint	Medication Required
1	X	X		
2	X		X	
3				
4				
5	X	X	X	X
6	X	X	X	X
7	X	X		
8	X	X	X	
9	X	X	X	X
10	X		X	X
11	X	X	X	X
12	X		X	X
13	X	X	X	X
14	X	X	X	
15	X	X	X	X
16	X	X	X	X
17	X	X	X	X
18	X	X	X	X
19				
20	X	X	X	X
21	X	X	X	
n (%)	18 (86)	15 (71)	16 (76)	12 (57)

Specific Medications Used Included:

Headache Medications	N
Acetaminophen/Aspirin/Caffeine	8
Rizatriptan	5
Sumatriptan	1
Butalbital/Acetaminophen/Caffeine	1
Gabapentin	4
Propranolol	2
Topiramate	1
Amitriptyline	1
Riboflavin	2

Sleep Medications	N
Melatonin	10
Doxepin	6
Gabapentin	6
Trazodone	3

Medications were selected based on clinical indication, efficacy, and tolerance, and were adjusted as clinically indicated. Efforts were made to minimize cognitive side effects

Neuroimaging

Conventional MRI sequences were acquired at 3T

- Including high resolution sagittal 3-dimensional MP-RAGE, T2 SPACE and FLAIR SPACE, coronal 2-dimensional T2-weighted imaging, axial 2-dimensional diffusion-weightedimaging, and axial T2*gradient echo

Results:

- As is common with mTBI or concussion, most patients had conventional imaging findings within normal limits
- Nine individuals (43%) had a few small nonspecific T2-white matter hyper-intensities (WMH's)
    - Three patients had multiple T2-WMH's more than expected for age
        - 2 mild, 1 moderate

Neuroimaging

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Results:

- As is common with mTBI or concussion, most patients had conventional imaging findings within normal limits
- Nine individuals (43%) had a few small nonspecific T2-white matter hyper-intensities (WMH's)
    - Three patients had multiple T2-WMH's more than expected for age
        - 2 mild, 1 moderate

NOTE: This does not include advanced structural / functional neuroimaging analysis

Audience Response Question #2:

Question

- Nearly all patients reported persistent neurological symptoms over three months post exposure.
  A. True
  B. False

Outline

- Introduction / Background / Timeline
- Exposure reports
- Neurological Manifestations
- **Neurological Rehabilitation: approach and preliminary response**
- Future Directions

Neurological Rehabilitation

- Individualized rehabilitation programs developed – based on clinical indications
  - Vestibular Physical therapy (n=17, 81%)
  - Neuro-Optometric Rehabilitation (n=14, 67%)
  - Cognitive Rehabilitation w/ OT or SLP (n=13, 62%)

- Patients requiring multiple therapies were held from work
  - N=14, 67%

Neurological Rehabilitation

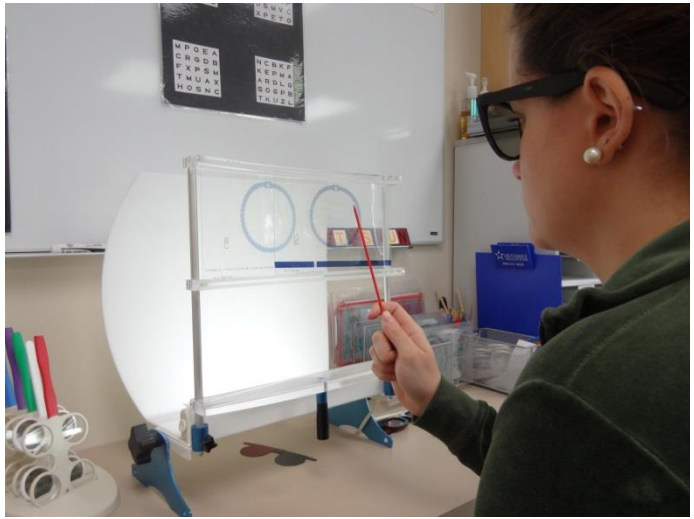
Vestibular Therapy

- Balance retraining
- Static and dynamic postural control with substitution via visual and somatosensory systems
- gaze stabilization (VOR), smooth pursuit and saccadic eye movement exercises
- Habituation

Neurological Rehabilitation

Neuro-optometric Rehabilitation

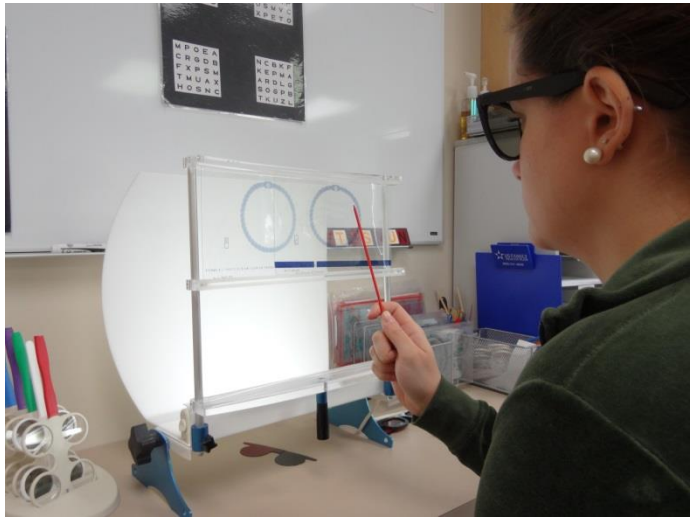
- Manipulation of vergence, accommodation and pursuits/saccades using prisms, 3D stereograms, 3D software, lenses and other instruments
- Designed to increase the speed, accuracy and amplitude of ocular motor skills, and reduce visual symptoms
- Lenses, prisms, tints



Neurological Rehabilitation

Neuro-optometric Rehabilitation

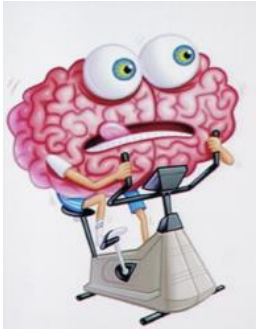
- Manipulation of vergence, accommodation and pursuits/saccades using prisms, 3D stereograms, 3D software, lenses and other instruments
- Designed to increase the speed, accuracy and amplitude of ocular motor skills, and reduce visual symptoms
- Lenses, prisms, tints
- Rehabilitation for abnormal smooth pursuit and saccadic dysfunction was coordinated between neuro-optometric rehabilitation, vestibular PT and OT



Neurological Rehabilitation

Cognitive Rehabilitation

- Neuropsychological testing
- Formal cognitive rehabilitation program
  - Occupational therapy and/or speech language pathology
- A combination of remediation and compensation to facilitate functional improvement
- Energy Management Strategies

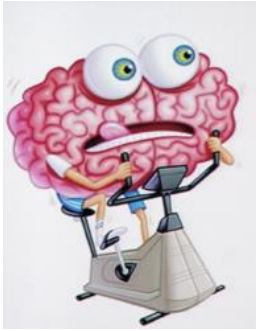


Neurological Rehabilitation

Cognitive Rehabilitation

- Neuropsychological testing
- Formal cognitive rehabilitation program
  - Occupational therapy and/or speech language pathology
- A combination of remediation and compensation to facilitate functional improvement
- Energy Management Strategies

- SLP →addresses cognitive-communication deficits by providing intervention in the areas of attention, memory, problem solving, organization and executive functioning

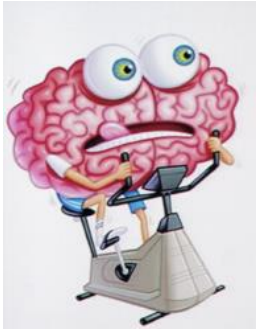


Neurological Rehabilitation

Cognitive Rehabilitation

- Neuropsychological testing
- Formal cognitive rehabilitation program
  - Occupational therapy and/or speech language pathology
- A combination of remediation and compensation to facilitate functional improvement
- Energy Management Strategies

- SLP →addresses cognitive-communication deficits by providing intervention in the areas of attention, memory, problem solving, organization and executive functioning
- OT → addresses these performance skills embedded in functional activities



Neurological Rehabilitation

Graduated Return to Work (RTW)

- 14 individuals initially held from work

- As of 2/15/18
  - 7 of those 14 had transitioned to a graduated RTW program
  - With accommodations / restrictions in place
  - While still undergoing higher-level, work-focused cognitive rehabilitation

Audience Response Question #3:

Question

- Rehabilitation of dysfunctional pursuit and saccadic eye movements, along with visual motion sensitivity is most effective when there is a multi-disciplinary approach to treatment, including vestibular, occupational and neuro-optometric rehabilitation.
  A. True
  B. False

Outline

- Introduction / Background / Timeline
- Exposure reports
- Neurological Manifestations
- Neurological Rehabilitation: approach and preliminary response
- **Future Directions**

Future Directions

- Continue clinical care
  - Long term monitoring of existing patients
  - Evaluation of additional cases as indicated
- Advanced neuroimaging analysis
- Develop operational diagnostic criteria (combo of clinical and imaging data)
- Potential blood-based biomarkers
- Epidemiologic analysis
- Collaborate with USG on basic science / technical aspects of exposure

Acknowledgements

- Physical Medicine & Rehabilitation — Stephen Hampton, MD, Timothy Dillingham, MD
- Occupational Medicine — Judith Green-McKenzie, MD
- Neurology — Ramon Diaz-Arrastia, MD, PhD; Danielle Sandsmark, MD, PhD
- Neurosurgery — Douglas H. Smith, MD; M. Sean Grady, MD
- Neuroradiology / Radiology — Ronald Wolf, MD, PhD; Ragini Verma, PhD
- Neuropsychology — Rosette Biester, PhD; Nora Johnson, PsyD
- Neuro-Optometry — Michael Gallaway, OD
- Vestibular Physical Therapy — Diana Duda, PT, DPT
- Occupational Therapy — Mary-Fran Madden, OTR/L, CBIS,MSCS
- Speech Language Pathology — Darlene Mancini, CCC-SLP
- Neuro-Ophthalmology — Grant Liu, MD, PhD
- Audiology / Otorhinolaryngology — Sherrie Davis, AuD; Michael J. Ruckenstein, MD
- Sleep Medicine — Charles Bae, MD; David Raizen, MD, PhD; Sharon Schutte-Rodin, MD
- Epidemiology / Biostatistics — Douglas J. Wiebe, PhD

- All of our administrative colleagues working behind the scenes
- All of our unmentioned collaborators outside of Penn